The limitations of Claims 1, 3 and 6 have been combined into new Claim 11, with the additional limitation that the alcohol co-solvent is now recited as being selected from the group consisting of ethanol, propylene glycol and glycerol, as disclosed in the specification at page 4, line 25. Also, the limitation that the cyclodextrin has an M.S. in the range of 0.3 to 3 and contains less than 5% unsubstituted β-cyclodextrin, as disclosed on page 3, lines 9 and 26, has been added. Claim 3 has been amended to delete limitations that are now redundant in view of the amended broad claim, and to correct its dependency. Claims 8 and 9 have also been amended to correct their dependency.

In view of the amendments to the claims, it is respectfully submitted that the Section 112 rejection has been overcome. Favorable reconsideration and withdrawal of this rejection is respectfully requested.

Claims 3-5, 7-9 and 11 are in the application. (In the Office Action, Claim 9 was not mentioned; it is assumed that this was an oversight.) All the claims have been rejected under 35 U.S.C. § 103 over Hostetler et al., "Effect of Cyclodextrin on the Pharmacology of Antifungal Oral Azoles", in combination with Heeres et al., WO 93/19061, and Heeres et al., U.S. Patent No. 4,916,134. this rejection is respectfully traversed, for the reasons that are set forth below.

It is first respectfully pointed out that Heeres et al., WO 93/19061, is not prior art to this application. Applicants are entitled to the filing date of September 30, 1993, the filing date of U.S. patent application Serial No. 08/129,504. This Heeres et al. reference was published on September 30, 1993, the same day, and is therefore not prior art to Applicants. The Examiner is informed that a U.S. equivalent of WO 93/19061 is pending as application Serial No. 08/295,885, filed on January 26, 1995, claiming the benefit of U.S. application Serial No. 07/853,648, filed on March 18, 1992. Serial No. 08/295,885 is assigned to the same assignee as this application. As far as the undersigned Attorney for Applicants is aware, the earliest publication date of the series of applications to which WO 93/19061 belongs was September 30, 1993.

The present invention is concerned with the provision of palatable and effective oral solutions of itraconazole and saperconazole. It has bee found that the best way to achieve this is to use a combination of a high intensity sweetener, such as saccharin or sucralose, along with a bulk sweetener, such as sorbitol or sucrose. It is submitted that the references do not teach or suggest this contribution to the art. Hostetler et al. are concerned with preparing aqueous oral solutions of saperconazole and itraconazole (one version of which uses hydroxypropyl-β-cyclodextrin ["HPC"] in an acidified solution that also contains propylene glycol). The purpose of the experiment was to determine the effectiveness of HPC in increasing the serum concentration of the active ingredient. The

solutions were administered to mice by "gavage", which means that the mice were force fed, probably through a tube directly into the stomach. Thus, the investigators here were not concerned at all with the palatability of the solutions; their sole concern was to compare the bioavailability of the active ingredient from various vehicles. As a practical matter, when a medicine is to be administered orally in the "real world" (as opposed to being administered forcibly to test animals in a lab), palatability is a significant factor to be considered. It has not proven to be an easy matter to prepare an itraconazole or saperconazole oral solution that was palatable. Applicants have discovered that a combination of a high intensity sweetener and a bulk sweetener is an excellent way to achieve palatability.

Hostetler et al. were not at all concerned with the palatability of the oral solutions they tested. Since they were not concerned with the problem, it is clear that they did not teach or suggest its solution. Heeres et al., WO 93/19061, even if it were available as a reference (which it is not), insofar as it is relevant to the issues herein, teaches even less than Hostetler et al. This Heeres et al. reference simply discloses aqueous solutions of itraconazole or saperconazole (or various stereoisomers thereof). Again, palatability was not a concern in this patent publication; solubility of the active ingredients was the sole concern. The Heeres et al. patent, No. 4,916,134 (the '134 patent), discloses oral solutions of saperconazole (see Examples 12 and 13) that do contain sweeteners and flavoring

agents. However, there is no disclosure in the '134 patent of saperconazole solutions containing HPC. Thus, the problems associated with imparting palatability to a drug solution containing HPC was not a concern in this patent. It is urged, therefore, that the '134 patent also fails to add a suggestion of the subject claimed invention to the teachings of Hostetler et al.

For the reasons that are set forth above, and in view of the present amendments to the claims, it is respectfully submitted that the rejection of all the claims under 35 U.S.C. § 103 over Hostetler et al., "Effect of Cyclodextrin on the Pharmacology of Antifungal Oral Azoles", in combination with Heeres et al., WO 93/19061, and Heeres et al., U.S. Patent No. 4,916,134, is in error. Favorable reconsideration and withdrawal of this rejection is respectfully requested.

In view of the foregoing amendments and remarks, it is urged that this application is in condition for allowance. Early favorable action is respectfully requested.

Respectfully submitted,

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